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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/656,084	09/06/2000	Barry N. Kreiswirth	19124.0002	8869

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EXAMINER	
LY, CHEYNE D	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/656,084	KREISWIRTH ET AL.	
	Examiner	Art Unit	
	Cheyne D Ly	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36 and 42-44* is/are pending in the application.

4a) Of the above claim(s) *42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36 and 44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1,3-5,7,8,10-14,16,17,21-36 and 42-44* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *February 11, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 11, 2004 has been entered.

2. The addition of new claims 42-44 has been acknowledged.

3. Newly submitted claims 42 and 43 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The new limitation of "determining the phylogenetic relatedness...based on...insertions and deletions of individual nucleotides;...repeat cassettes" causes the new claims to be distinct from the elected claimed subject matter. It is acknowledged that claims 16 and 17 comprise the limitation of insertion and deletion of a repeat sequence, or individual nucleotide; however, said limitations are distinct from the step of "determining the phylogenetic relatedness...based on...insertions and deletions of individual nucleotides;...repeat cassettes" as recited in claims 42 and 43. The distinct inventions support the lack of overlapping searches which documents the undue search burden if they were search together.

4. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 42 and 43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

5. Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 are examined on the merits.

CLAIM REJECTIONS - 35 U.S.C. § 112, FIRST PARAGRAPH

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

8. NEW MATTER REJECTION.

9. Specific to claim 1, line 6; claim 32, lines 11-12; and claim 33, line 7, the limitation of first region comprising a variable number of tandem repeats (VNTRs) is considered to be new matter. It is acknowledged the instant specification discloses VNTR on page 21, lines 11-16. Further, the instant specification has disclosed the first region comprising a generic repeating sequences of nucleotides. However, the specification does not disclose the limitation of said first region comprising a variable number of tandem repeats (VNTRs). Therefore, the limitation of first region comprising VNTRs does not have written description basis as originally filed.

10. Specific to claim 1, lines 11-12; and claim 33, line 11, the limitation of "at least two of the plurality of samples" is considered to be new matter. It is acknowledged that the instant specification discloses "comparing two isolates" (page 30, line 7) is different from the limitation of "at least two of the plurality of samples" in regard to written description basis as originally

filed. For example, the limitation of "at least two of the plurality of samples" includes two samples or more, and the disclosure of "comparing two isolates" is exactly two.

11. Specific to claim 27, lines 2-6, the limitation of "warning includes:...having an outbreak problem" is considered to be new matter. It is acknowledged that the instant specification discloses "Server 188 notifies the hospital...or a dialysis machine in the burn ward" (page 27, line 15 to page 28, line 2) which is different from the limitation of "transmitting ...to each location having an outbreak problem".

CLAIM REJECTIONS - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1, 3-5, 7, 12-14, 16, 17, 21, 25-34, 36, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sloane (US 5,619,991A) taken with Hoe et al. (1999) in combination with Belkum et al. (1997).

RESPONSE TO ARGUMENT

15. Applicant's arguments as directed to Hoe et al. have been fully considered and responded to via the citation of the Sloane and Belkum et al. references below.

16. Sloane discloses improvements in the method of treating diseases, and identifying and tracking epidemiological events and/or trends (outbreak) (Abstract etc. and column 1, line 39 to column 2, line 12). The method of Sloane comprises an epidemiological database computer facility, which collects data from plurality of locations (hospitals and other institutions with medical facilities) and wherein said data comprise various medical, personal and epidemiological data relevant to a patient (column 2, lines 13-24).

17. The network system of Sloane comprises epidemiological database computer facility (centralized database), remote facilities (PC and servers) connected to said network, and exchanges of electronic communications between systems within said network (Figure 1 and column 2, lines 40-59), as in instant claim 32, lines 1-9, and claim 44, line 4.

18. The epidemiological database computer facility correlates epidemiological information of a specific location it receives over time (tracking spread) and returns an electronic message to an e-doc indication the source of disease (column 2, lines 26-39), as in instant claim 1, lines 20-22.

19. The epidemiological database computer facility monitors for the known signatures of particular respective diseases of epidemiological interest, e.g. influenza, tuberculosis etc., identifies the geographical distribution, and reporting/suggesting treatment modalities for such

diseases (warning and control) (column 8, lines 2-12). The database record includes patient identification number (ID), name, and address (physical location) (column 6, lines 52-59), as in claim 1, lines 8-10.

20. However, Sloane does not disclose the limitation of tracking spread of infectious bacteria by sequencing a first region comprising the VNTR sequences. It is noted that the improvement of an epidemiological database computer facility of Sloane, which collects data from plurality of locations (hospitals and other institutions with medical facilities) and wherein said data comprise various medical, personal and epidemiological data relevant to a patient (column 2, lines 13-24) are directed to any medical data related to an epidemiological event including sequence data.

21. Belkum et al. discloses the importance of VNTR sequences for tracking outbreaks of infectious bacteria such as *Staphylococcus aureus* wherein the coagulase and protein A genes are clearly polymorphic in their repetitive regions (Belkum et al., page 2017, Abstract etc. and column 1, lines 1-29), as in instant claim 1, lines 5-6, claim 7, and claim 32, line 12.

22. Belkum et al. discloses the identification of VNTR sequences are directed to specific patients (Table 1), as in instant claim 1, lines 18-19.

23. Hoe et al. discloses a method for tracking pathogenic microbial species in an epidemiologic investigation of putative disease outbreaks (page 254, column 1, lines 1-14) and providing insight to the virulence of the said microbial species (page 261, column 1, lines 51-53 to column 2, lines 1-15), as in instant claims 25-27.

24. The method of Hoe et al. comprises sequencing the sic gene wherein a region contains repeat sequences to unambiguously differentiate 30 M1 isolates (plurality of bacterium samples) recovered from 28 patients in Texas (Abstract etc.). The sequenced nucleic acid molecules are

used to search an emm database maintained in the laboratory (page 255, column 2, Sequence Analysis of emm §, lines 3-10 and Figure 4), as in instant claim 1, lines 3-7, claims 28-30, and claim 44, lines 2-3.

25. "For molecular analysis of the GAS causing recent cases, 100 isolates were sent to a laboratory at Baylor College of Medicine (infection control facility) (page 255, column 2, lines 8-11). M1 isolates cultured from patients share a common ancestor (phylogenetically related) and lack readily detectable chromosomal variation (page 254, column 2, lines 2-13 and Figure 1), as in instant claim 1, lines 11-19, claim 32, lines 9-1, and claims 5, 12, and 36.

26. Each allele is characterized by single nucleotide changes resulting in single amino acid substitutions in the resulting M1 protein (page 256, column 1, lines 12-15) and eight new nucleotide substitutions were identified in eight codons, and one codon had a new dinucleotide change (sequence) (page 257, column 1, lines 14-21), as in claims 16 and 17.

27. The M1 isolates includes twenty-three Texas isolates had allele *emm1.0* (local and regional) the most common *emm1* allele in M1 isolates globally (Figure 1, page 256, column 1, lines 1-20, and Table), as in instant claim 21.

28. It is noted that the laboratory of Hoe et al. is located in Texas, therefore, suggests that the database and the location where the sample is obtained from patients in Texas are in the same location (page 255, column 2, lines 8-11), as in instant claim 4.

29. Further, the database contains sequences from global sources (page 255, lines 28-30) and GenBank, Bethesda, MD, (Figure 1) which is remote from the location where the location of the samples are obtained, as in instant claim 3.

30. The inclusion of a document by Benson et al. is not used as prior art but only to disclose that sequences from GenBank are transmitted via a network from a remote facility with a centralized database (page 4, column 1, Building The Database § and Figure 3) and transmission exchanges occur between research remote infection control facility such as Baylor College of Medicine (Hoe et al., Figure 1) and NCBI (Benson et al., BLAST sequence similarity searching §), as in instant claim 32, lines 16-20.

31. The submission of sequences from sequencing centers and authors who submit data directly to the collaborating databases (store in a database) (Benson et al., page 4, column 1, Building The Database §, 1-7), as in instant claim 1, lines 8-10, and claim 32, lines 13-15.

32. Further, Benson et al. discloses the GenBank and Entrez are available over the Internet in a client server version or GenBank in a CD-ROM (Benson et al., page 5, column 1, lines 14-32), as in instant claim 33.

33. The sample of Hoe et al. is amplified by PCR and sequenced using oligonucleotide primers (Hoe et al., page 258, column 1, lines 1-7; and page 259, PCR and Sequence Analysis of a Polymorphic Direct Repeat (DR) Chromosomal Region §), as in instant claims 13 and 14.

34. Hoe et al. further discloses, "lack of readily available detectable chromosomal variation has limited insights on the molecular origin of new virulent strains" (page 254, column 2, lines 7-13), which suggests slowly mutating nucleic acid region. "Stockbauer et al. Analyzed 165 M1 isolates from diverse localities...and documented a uniquely high level of allelic variation" (page 255, column 1, lines 1-4), which suggests more rapidly mutating nucleic acid region. Therefore, the disclosure above suggests tracking of infection based on slowly and rapidly mutating nucleic acid region as in instant claim 31.

35. Hoe et al. discloses many sic alleles are confined to local geographic areas, however, several alleles were found among organisms cultured from patients in Mexico and former East Germany (Hoe et al., page 261, column 2, lines 16-23), as in instant claim 34.

36. An artisan of ordinary skill in the art at the time of the instant invention would have been motivated by the improvements of Sloane in the method of treating diseases, and identifying and tracking epidemiological events and/or trends (outbreak) (Abstract etc. and column 1, line 39 to column 2, line 12) to utilized said method with the outbreak tracking method directed to sequencing of Hoe et al. and VNTR medical data of Belkum et al. Therefore, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to use method of treating diseases, and identifying and tracking epidemiological events and/or trends (outbreak) as directed to sequencing medical data of Sloane, Hoe et al., and Belkum et al.

37. Claims 1, 3-5, 7, 8, 10-14, 16, 17, 21-36, and 44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sloane (US 5,619,991A) taken with Hoe et al. (1999) in combination with Belkum et al. (1997) in view of O'Brien et al (1997) and Paradiso et al. (PN US 6,404 340 B1).

38. Applicant's arguments as directed to Hoe et al., O'Brien et al., and Paradiso et al. have been fully considered and responded to via the citation of the Sloane and Belkum et al. references below.

39. Hoe et al. discloses the limitations of claims 1, 3-5, 7, 12-14, 16, 17, 21, 25-34, 36, and 44 as described above.

40. However, Hoe et al. does not disclose the limitations of claims 8, 10, 11, 22-24, 35, and 38.

41. O'Brien et al. teaches a method of comparing "genetic relatedness among Mycobacterium tuberculosis isolates recovered from patients with active disease" (Page 387, Column 2, Lines 2-5). Due to the tracking of patients' medical records by Bellevue Hospital and the Department of Health in New York City, patients found not adhering to therapy were quarantined (page 389 to 390, Case Report §). This displays tracking a patient's physical location as well as the sharing of patient information as recited in instant claims 11 and 22. Further, O'Brien et al. discloses a linked database of fingerprints from isolates in patients from New York City (page 391, column 1, 38-40), as in instant claim 23.

42. Patient is identified and patient sample analyzed prior confinement in the health care facility (page 389 to 390, Case Report §) as recited in instant claims 8, 35, and 38.

43. The "clinical and demographic features of these patients" (Page 390, column 2, 1st paragraph) were reviewed for population risk factors in addition to determining "ongoing transmission of tuberculosis" (Page 390, column 2, lines 1-19) as recited in claim 10.

44. Paradiso et al. discloses a method for sensing and tracking a patient's physical location during a medical treatment for a specific disease (column 2, lines 32-49), as instant claim and 24.

45. It is noted that the improvement of Sloane of an epidemiological database computer facility, which collects data from plurality of locations (hospitals and other institutions with medical facilities) and wherein said data comprise various medical, personal and epidemiological data relevant to a patient (column 2, lines 13-24) are directed to any medical data directed to a

patient. Therefore, the improvement of Sloane is directly applicable to method of tracking disease outbreaks of O'Brien and patients of Paradiso et al.

46. One of ordinary skill in the art at the time of the instant invention would have been motivated by the improvements disclosed by Sloane to track outbreaks of diseases by tracking infected patients in the outbreak as taught by O'Brien and Paradiso et al. Therefore, it would have been obvious to one of ordinary skill in the art to perform the method of tracking outbreaks as taught by Sloane, Hoe et al., and Belkum et al., and by tracking infected patients in said outbreaks as taught by O'Brien and Paradiso et al.

CONCLUSION

47. Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 193), and 1157 OG 94 (December 28, 1993) (see 37 CFR § 1.6(d)). The CM1 Fax Center number is (703) 872-9306.

48. Any inquiry concerning this communication or earlier communications from the examiner should be directed to C. Dune Ly, whose telephone number is (571) 272-0716. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

49. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, Ph.D., can be reached on (571) 272-0722.

50. Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner, Tina Plunkett, whose telephone number is (571) 272-0549.

C. Dune Ly
4/8/04

ARDIN H. MARSCHEL
PRIMARY EXAMINER
4/11/04